FIRST OFFICE ACTION

Applicant's amendment of 4-6-06 has been acknowledged and entered. Claims 1-45 are pending.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1, in the definition of R^8 and R^9, the phrase "together form" is recited twice.

b. Claims 2-7 and 9 recite the term "preferably" which indicates the situation of "broad limitation followed by narrow limitation".

c. Claims 16, 21, 36, 38, 44 and 45 recite the limitation of "infectious diseases, including opportunistic diseases" which also indicates the situation of "broad limitation followed by narrow limitation".

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection

desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of ***Ex parte Steigewald***, 131 USPQ 74 (Bd. App. 1961); ***Ex parte Hall***, 83 USPQ 38 (Bd. App. 1948); and ***Ex parte Hasche***, 86 USPQ 481 (Bd. App. 1949).

d. **Use Claims:** Claims 15-33 provide for the use of a compound of formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Use Claims: Claims 15-33 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper

definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example ***Ex parte Dunki***, 153 USPQ 678 (Bd.App. 1967) and ***Clinical Products, Ltd.* v. *Brenner***, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablement:** Claims 36-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating HCMV (human cytomegalovirus), does not reasonably provide enablement for treating or preventing infectious diseases including opportunistic infections such as those caused by herpes virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claims 36-45 recite a method of treating or preventing infectious diseases including opportunistic infections such as those caused by herpes virus (specifically, herpes simplex viruses, varicello viruses, cytomegalo viruses, muromegalo viruses, roseolo viruses, lymphocrypto viruses and rhadino viruses). Said viruses cause various infections in several parts of the body and manifest in different ways. Thus, the scope of the above claims is unduly broad.

The amount of direction or guidance presented: The specification describes bioassay to determine the antiviral activity of the claimed compounds. Specifically, the bioassay looked at the activity of the claimed compound on the viral kinase UL-97 isolated from HCMV. The IC_{50} values were determined, and they ranged from 0.02μM to 1.2μM. However, the data of "Viability [%] at 10μM" does not seem to be correlated with the data of "UL 97 IC 50 [μM]". For example, the data for compound 2 showed that only **0.4μM** of said compound was needed to inhibit 50% of UL97 (i.e., IC 50 is 0.4μM), but at **10μM** (or 25x IC50 value) of said compound, the viral viability was 98%. Thus, it appears that UL97 might not have been the kinase that had been necessary for HCMV to survive.

Regarding the test for inhibiting replication of HCMV, and plaque reduction, a few of the claimed compounds showed IC_{50} values of 2 - 6μM. Thus, as far as HCMV is concerned, the claimed compounds showed efficacy, but for other viruses the existing data could not be extrapolated due to different viral morphology.

The state of the prior art: While many commercially available antiviral agents like acyclovir can treat viruses such as herpes zoster (or shingles), and other can treat AIDS (like Zidovudine, Lamivudine, Tenofovir DF, etc.), they are not known to treat HCMV. The only commercially available drug that treats HCMV is Fomivirsen (or Vitravene), but it does not share the same heterocyclic backbone with other antiviral agents, and is not used to treat HIV or other viruses. Thus, the state of the art does not support a method of treating or preventing infectious diseases in general.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select an effective compound from the large Markush group of formula I. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic profile for each compound. Given a large Markush group of the claimed formula I, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting path ways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the claimed compounds only showed inhibition on HCMV and no other viruses. There is no correlation between different viral morphologies to warrant that the claimed compounds could also inhibit a wide range of viruses.

See ***Hoffman v. Klaus*** 9 USPQ 2d 1657, and ***Ex parte Powers*** 220 USPQ 925 regarding type of testing needed to support *in vivo* uses.

Note, the Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the **full scope** of the invention without 'undue experimentation'".

Thus, given the unpredictable nature of the art, and the vast number of compounds claimed herein, one skilled in the art will have to carry out undue experimentation to practice the method of treatment recited in above claims.

Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. Note, substantiation of utility and its scope is required when utility is "speculative", or "sufficiently unusual". See ***Ex parte Jovanovics***, 211 USPQ 907, 909; ***In re Langer*** 183 USPQ 288. Also, see ***Hoffman v. Klaus*** 9 USPQ 2d 1657, and ***Ex parte Powers*** 220 USPQ 925 regarding type of testing needed to support *in vivo* uses.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-5 and 7-14 are rejected under 35 U.S.C. 102(b) as being anticipated by **Uckun et. al.** (US 6,080,747). On column 20, Table 1 lists the following compounds that read on the instant formula I with the following substituents:

i. R^1 is hydrogen;

ii. R^2 is hydrogen;

iii. R^7-R^9 and R^{11} are hydrogen; and R^{10} is a halogen or hydroxy;

iv. Or, R^7 and R^9-R^{11} are hydrogen, and R^8 is a halogen or hydroxyl;

v. R^4 and R^5 are methoxy groups.

In particular, compound VHI-P79 reads on compound 12 of the instant claim 13.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMTHOM N. TRUONG whose telephone number is (571)272-0676. The examiner can normally be reached on Monday thru Friday (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Tamthom N. Truong/
Examiner, Art Unit 1624

/JAMES O. WILSON/
Supervisory Patent Examiner, Art Unit 1624

7-22-10